SOCIETÀ ITALIANA DI FARMACOLOGIA

MODELLO PER INVIO RELAZIONE DI METÀ E FINE PERIODO

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TIPOLOGIA DI BORSA RICEVUTA: Borsa SIF di ricerca per brevi periodi all'estero

TIPOLOGIA DI RELAZIONE (es.: metà periodo o finale): Relazione metà periodo

TITOLO DELLA RELAZIONE: Gut Microbiota, Neuropsychology and Young Binge Drinkers

RELAZIONE:

Background

Binge drinking (BD) is defined as the consumption of 4 drinks for women and 5 drinks for men in about 2 hours (at least once per month), leading to a blood alcohol concentration ≥ 0.8 g/L[1,2]. Among young people, BD is emerging as a prevalent pattern of heavy alcohol consumption[3]. Alcohol misuse is an important social and economic issue and has been highlighted as a public health priority by the European Commission.

Brain structural and functional anomalies (*e.g.* lower volume in prefrontal, hippocampal and cerebellar areas) and neuropsychological deficits in executive functions, memory or emotional difficulties, have been demonstrated in binge drinkers[4]. All together these factors are associated with a high risk of developing an alcohol addiction.

Growing evidence indicates that chronic alcohol consumption could induce neuro-inflammation, not only from a direct interaction with the brain but also from peripheral sources, particularly from the gut and its resident microbial complex. Indeed, several studies are demonstrating that the microbiota-gut-brain axis, a bi-directional network that involves neural, immune and endocrine pathways, could play a major role in the pathophysiology of mood disorders, stress response, and alcohol dependence[5,6].

In rodents and humans, chronic alcoholism has been linked with increased intestinal permeability and alterations of gut microbial composition, with a decrease in global abundance of bacteria and specific reductions of anti-inflammatory microbial strains, causing elevation of peripheral cytokines and sensitization of the neuro-immune system to ethanol[4,7].

Human studies with young binge drinkers have shown that even a single BD episode can increase peripheral endotoxin levels, and a regular BD pattern was associated with alterations in cortisol levels and peripheral inflammatory markers (*e.g.* lipopolysaccharide [LPS] and interleukin [IL]-6), related with poor memory and executive functions[8]. These inflammatory pathways could be well-matched with alterations in the microbiota-gut-brain axis. Anyway, no study to date has investigated the gut microbiota in young people with a frequent pattern of alcohol intoxication.

Aim of the study

The main aim of this study is to identify new biomarkers of dysfunction by exploring the gut-microbial composition, immune and stress alterations in BDs and their neurocognitive correlates. The study will examine the gut microbiota and cognitive/affective variables, to further understand the microbiota-gut-brain axis communication, in young people with different alcohol consumption patterns. Moreover, immune/inflammatory markers will be analyzed in the blood, together withacute (saliva) and chronic (hair) cortisol levels as an index of the hypothalamic-pituitary adrenal (HPA) activity.

Ongoing results

In these first three months more than 40 participants (age range 18-22 years) have been pre-screened and 19 of them completed the two-scheduled visits. Enrollment is still ongoing to reach a representative sample.

Demographic data (comprising age, sex, race), current medical history, family medical history (including alcoholism history) and medication use have been collected. Moreover, participants completed a range of self-report questionnaires regarding current/previous psychopathological and gastrointestinal symptoms, sleep quality, physical activity, dietary intake and their alcohol/drug use patterns.

Subsequently, several biologic samples have been collected: stool samples for microbiota composition and short chain fatty acids analysis and urine samples for metabolomics. Among other aspects, blood samples will be used to determine stress levels and the inflammatory profile (including peripheral stimulation with Toll-like receptor [TLR] agonists-induced cytokine release), and hair and saliva to determine chronic and acute cortisol levels, respectively.

Finally, cognition has been analysed using the Cambridge Neuropsychological Test Automated Battery (CANTAB), a computerised neuropsychological test battery, specifically tasks that involve memory, inhibition, decision making and emotional functioning were administered.

In the next months, more participants will be enrolled and enzyme-linked immunosorbent assays (ELISA) will be performed to analyse cytokine levels in blood supernatants and cortisol concentration in saliva. Plasma tryptophan, kynurenine and kynurenine acid will be measured using high performance liquid chromatography coupled to sequential fluorescence and UV detection. Finally, urine samples for metabolomics will be analysed by high performance liquid chromatography and DNA/RNA will be purified from stool samples and then analysed.

References

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La Società Italiana di Farmacologia dichiara che i dati personali comunicati dall'utente sono trattati in conformità alle disposizioni del D. Lgs. 196/2003, così come modificato dal D. Lgs. 101/2018, ed alla normativa comunitaria (Regolamento UE 2016/679) secondo quanto indicato specificamente nell'informativa privacy reperibile sul sito internet della Società all'indirizzo: https://sif-website.s3.amazonaws.com/uploads/attachment/file/240/Informativa_Privacy_SIF_Generica.pdf che l'utente, con la sottoscrizione del presente Contratto, dichiara di aver compiutamente visionato, compreso e accettato.

Data ____01-05-2019_____ Firma _____